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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/667,796	09/22/00	CURTIS W	99-2175

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INTELLECTUAL PROPERTY OFFICE
THE PENNSYLVANIA STATE UNIVERSITY
113 TECHNOLOGY CENTER
UNIVERSITY PARK PA 16802

EXAMINER	
SORBELLO,E	
ART UNIT	PAPER NUMBER
1633	6

DATE MAILED: 10/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/667,796	CURTIS, WAYNE R.	
	Examiner	Art Unit	
	Eleanor sorbello	1633	

-- Th MAILING DATE of this communication appears on th cover sheet with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 3 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing a polypeptide in a dicotyledonous plant tissue, wherein the plant tissue is a root culture by adding *Agrobacterium tumifaciens* or *Agrobacterium rhizogenes* encoding the polypeptide of interest wherein *Agrobacterium tumifaciens* and *Agrobacterium rhizogenes* are auxotrophic and the timing of the addition of the Agrobacterium to the bioreactor is specific and product formation is specifically timed in order that high titers of product are obtained, **does not** reasonably provide enablement for a method of producing a polypeptide in any monocotyledonous plant tissue or algal tissue, by the aforesaid methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The invention is directed to methods of making a polypeptide or protein in a plant tissue by adding the plant tissue which may be any part of a monocotylendous or dicotyledonous plant or algal suspension to a bioreactor to which any species of Agrobacterium is added wherein the bioreactor contains between 50ml to about 10,000

cells. Further limitations encompass the use of Agrobacterium which is an auxotroph. Still further limitations recite that the Agrobacterium is to be added to the plant material in the bioreactor at about 7 to about 14 days of growing the plant culture in the bioreactor and that the length of reaction time between the plant culture and Agrobacterium is about 1 to about 4 days.

The specification teaches extraction of protein from a root culture of a dicotyledonous higher plant by the addition of a mutated form of Agrobacterium in order to eliminate problems of bacterial overgrowth due to excess amount of nutrients in the plant media. Therefore, applicants taught the purpose of using "nutritionally impaired" Agrobacterium which provides control over the co-culture growth. Applicants taught methods of mutating the Agrobacterium chromosome using a Tn5 mutagenesis vector. The specification teaches that auxotrophic Agrobacterium were added to cultures of actively growing Nicotina glutinosa roots and N. tabacum BY2 cells and indicates that control of Agrobacterium growth in co-culture can be achieved. Additionally the specification teaches that specific auxotrophs are better for roots and others for cells. The specification also teaches that the addition of pyrene butyric acid (PBA) to the chemical media was a way of developing Hyoscyamus muticus plant roots grow with or without root hairs and applicants taught that the cell lines with profuse root hairs when disrupted showed a much higher level of transient recombinant polypeptide expression.

Lorz et al.(1985) teach that the Agrobacterium tumefaciens which is a natural vector for plants represents the most efficient system for gene transfer into higher plant cells. However the host range of Agrobacterium is limited because Agrobacterium

infection of cereal crops or other Gramineae species have been difficult. (See introduction page 178). Lippincott et al. (1978) underscore that stated by Lorz et al. in that Agrobacterium infects monocotyledenous and dicotyledenous plants very differently and that the Agrobacterium enters via attachment to the cell wall, and that if the cell wall is inhibitory, entry and therefore transformation will not take place. (See Abstract). More recently Baszczynski et. al. (U.S. Pat. No: 6,300,545 B1) teach infection of monocotyledonous plants based on methods taught by Heath et al. and Grimsley et al. (See U.S. Pat. No: 6,300,545 B1, col. 2, lines 15-20; col. 16) which incorporates specific innovative steps not directly extrapolatable from that used for dicotyledonous plants.

Applicants however, claim a method of producing a polypeptide from a monocotyledonous plant, and prophetically state that the same procedure may be used for corn etc. See page 27 of specification. It is not clear that the applicants provided any experimentation to support that which has not been straightforward as documented in the post filing art (unavailable at the time the instant application was filed) to work; especially in view of the specifics required by the bioreactor conditions as documented by applicants. In instances where the prior art does not teach one how to use the method of the instant invention as claimed, the specification has to be very detailed with support via experimentation that one of skill in the art will without undue experimentation be able to make and use the invention as claimed.

The claims broadly encompass any plant tissue including algae to be used as plant material to be introduced into the bioreactor to which the Agrobacterium is to be subsequently added at a specified time period. As stated above, the prior art does not

teach Agrobacterium infecting and transforming any algal tissue. As stated above, using different conditions, Agrobacterium has been found to transform monocotylendous plants such as corn more recently. Therefore in view of the claims directed to a method for recombinantly and transiently producing a polypeptide in a monocotyledonous plant under conditions not stated precisely in the specification, one of skill will require undue experimentation to use the invention as claimed. Given the limited host range of Agrobacterium and the lack of guidance in the specification regarding lower plant susceptibility, it is not clear that Agrobacterium will be able to infect lower plants such as algae. Applicants have not supported their claim that Agrobacterium will be able to transfect algal cells and therefore are not enabled for that which is claimed.

Therefore, in view of the state of the art, the breadth of the claims, the guidance in the specification and examples provided in the specification, one of skill in the art will require undue experimentation to make and use the invention as claimed.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (US. Pat. Nos: 5,550,038).

Goodman et al. teach plants as bioreactors producing polypeptides and proteins such as enzymes and antibodies. They teach that roots, leaves, stalk or the like can be used. They teach sterile tobacco plants stem-stab inoculated with A. tumefaciens resulting in the production of gall tissue which was transferred to kanamycin plates wherein considerable callus proliferation took place. Subsequently gall-induced callus material was harvested for mRNA and protein analysis. They also taught that in the transformed plant tissue a visible band ran at the same size as the positive control of γ-interferon.(See col. 8, lines 30-67 Pat. No; 5,550,038). They suggest that the transfer of a DNA construct into a plant cell may be by infection with A. tumefaciens or A. rhizogenes, microinjection, liposome fusion, viral infection or the like, however the particular manner of infection was not important. Goodman et al. suggest that both monocots and dicots may be used but teach only a method for producing mammalian peptides in dicotylenonous plant cells. The bioreactor used by Goodman et al. was a 5 ml tube, and they started the reaction with 1.6 or 1.0g of frozen tobacco tissue from tissue culture, the pH being 7.4. (See col. 9. U.S. Pat. No; 5,550,038). However, they added transformed plant cells into the bioreactor, and did not transform the plant cells in the bioreactor as the instant invention does. However, it is not clear that this different order of method steps confers any unanticipated results.

Sequence of steps ie. inoculation before or after addition of cells to the bioreactor is an obvious design choice.

Therefore, claims 1-18 are rejected as being obvious.

5. Claims 1, 13, 19, 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goodman et al. (US. Pat. Nos: 5,550,038) as applied to claims 1-18, in view of Baszczynski et al. (U.S. Pat. No: 6,303,341 B1).

The claims are rejected over Goodman as described above.

Goodman et al. however, did not use acetosyringone in their buffer.

Baszczynski et al. teach the usefulness of using acetosyringone in buffers for inducing infection of plant cells by bacteria such as Agrobacterium. (See col. 15, lines 62-67).

Therefore it would have been obvious at the time the invention was made to have included acetosyringone as an activator to induce infection of the plant cells by the Agrobacterium as taught by Baszynski et al. in the method of Goodman.

Claims 1, 13, 19, 20 are therefore rejected as being obvious.

Conclusion

6. Claims 1-20 are rejected.

7. Any inquiry concerning this communication should be directed to Eleanor Sorbello, who can be reached at (703)-308-6043. The examiner can normally be reached on Mondays-Fridays from 6.30 a.m. to 3.00 p.m. EST.

Questions of formal matters can be directed to the patent analyst,

Tracey Johnson, whose telephone number is (703) 305-2982.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark, can be reached on (703) 305-4051. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

If the claims are amended canceled and/or added the applicants are required to follow Amendment Practice under 37 CFR § 1.121 *(http://www.uspto.gov)* and A CLEAN COPY OF **ALL** PENDING CLAIMS IS REQUESTED to facilitate further examination.

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER